Master de Sciences et Technologies
Mention Biologie Intégrative et Physiologie
Parcours : Neurosciences
Responsable : Professeur Régis Lambert

Internship Proposal
Academic Year 2019-2020

1. Host team :

Research Unit (e.g. Department or Institute): Brain and Spine Institute, ICM
Inserm U1127, Sorbonne Université, CNRS UMR 7225
Research Unit Director: Alexis Brice
Research Team Director: Brahim NAIT OUMESMAR
Team name: Myelin Plasticity and Regeneration

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2. Internship project title:

Deciphering the function of axon-OPC synapses in myelination

3. Internship Description :

The main function of oligodendrocytes in the central nervous system (CNS) is to produce the myelin sheath, insulating axons and increasing the conduction velocity of action potentials. These cells are derived from oligodendrocyte precursor cells (OPCs), a class of progenitors highly abundant at birth, but also persistent in the adult CNS. By their capacity to generate oligodendrocytes, OPCs play a key role in developmental myelination and in myelin regeneration following injury during adulthood. It has been established that OPCs are synaptically innervated by glutamatergic and GABAergic axonal fibers throughout the CNS, demonstrating that synapses are not only a property of neurons. However, the role of axon-OPC synapses in oligodendrocyte development and myelination remain so far poorly understood.

To decipher the functional role of axon-OPC synapses in myelination, we are currently using the zebrafish as a model. The zebrafish larva is an ideal system for such studies as they develop externally and rapidly, are small, transparent and their CNS is relatively well characterized. The main objectives of this master 2 internship are: **1**) to characterize the synaptic connectivity between axons and OPCs in the embryonic zebrafish spinal cord and **2**) to determine the role of axon-OPC synapses in myelination. For this project, we recently generated several zebrafish lines expressing pre- and post-synaptic markers tagged with fluorescent reporters. Using these lines, this project aims to characterize the spatial and temporal distribution of axon-OPC synapses throughout oligodendrocyte development, evaluate their density and correlate these data with myelination, using time-lapse in vivo imaging. Next, we will selectively invalidate axon-OPC synapses using the CRISPR/Cas9 technology in the zebrafish larvae, and examine whether loss of synaptic activity in OPCs alters their proliferation, differentiation and myelination properties. Overall, this project should provide better insights into the mechanisms of activity-dependent regulation of myelination under physiological and pathological conditions.